

# Listing a Drug Product in SPL Format

SPL Release Four Training Session – Module 5

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# Transitioning from Paper to Electronic: Drug Registration and Listing

- If you list electronically list your product(s) do not list the same products using paper (FDA Form 2657 or FDA Form 2658)

# Transitioning from SPL R3 to R4

- GUIDs – Change case of uppercase letters to lower case.
- **IMPORTANT** – retain setID – just change the case of letters if uppercase is utilized.
- Delete coating and symbol product data elements from content of labeling/listing documents.
- Delete translation for units of measure for strength

# Transitioning from SPL R3 to R4

- Include a few more listing data elements
- Enter effectiveTime and version number prior to submitting to FDA

# Components of Drug Listing/Content of Labeling SPL

- Administrative
- Content of Labeling
- **Product data elements**

# Note

- Content of Labeling and Listing information for product(s) should be in the **same** file

# Administrative (Document Tracking Information)

## Basic information to identify the SPL document:

- **Document ID:** is a Globally Unique Identifier (GUID) and is unique for each version of the document. Letters used in a GUID are lower case.
- **Document Type:** The `<code>` is the LOINC code which provides information on the document type.
- **Effective Time:** provides a date reference to the SPL version including the year, month and day as yyyyymmdd.
- **SetID:** is a GUID and is a unique identifier for the document that remains constant through all versions/revisions of the document.
- **Version number:** is an integer greater than zero that provides a sequence to the versions of the document.

# Terminology

SPL Acceptable Terms



# Data Elements

- Data Element
  - A basic unit of identifiable and definable information. It occupies the space provided by a field in a record or a block on a form, and has an identifying name and value or values for expressing a specific fact. A data element is defined by its name, description, source, length, structure, and format.
- Product Data Elements
  - Formerly known as Drug Listing Data Elements
  - Drug listing data elements are **metadata** displayed via SPL stylesheet for purpose of review
  - Computer friendly information - product information which is tagged that permits search of key information.
  - Information system friendly – Medication information in computer readable form - Easily imported into information systems

# Terminology

- **Standard terminology** is used for SPL product data elements. Information about the controlled vocabulary for SPL is available at <http://www.fda.gov/oc/datacouncil/spl.html> under “SPL Terminology.”

# Terminology

- Product
  - Proprietary and nonproprietary name and code
- Description
  - Ingredients
    - Active and inactive ingredient and active moiety name and code (Unique Ingredient Identifier (UNII) from FDA Substance Registration System (SRS))
    - Active and inactive ingredient strength (National Cancer Institute (NCI) Thesaurus, Unified Codes for Units of Measure (UCUM))
    - Dosage form (NCI Thesaurus)
    - Appearance (imprint, color, shape, size, score, coating, symbol) (NCI Thesaurus and HL7)
    - Route of administration (NCI Thesaurus)
    - DEA schedule (NCI Thesaurus)
- Packaging
  - Package type (NCI Thesaurus), quantity and packaging code

# Ingredients (Terminology)

- Ingredient name (substance name)
  - SRS preferred name of ingredient (active and inactive)
  - Source – FDA SRS
- Ingredient code (substance code)
  - Unique Ingredient Identifier
  - Source –FDA SRS
- Active moiety name (active moiety entity name)
  - active ingredient or portion of active ingredient without counter ion (if relevant)
  - Source –FDA SRS
- Active moiety code (active moiety code)
  - Unique Ingredient Identifier (UNII)
  - Source –FDA SRS

# Unique Ingredient Identifier (UNII)

- Joint FDA/USP Substance Registration System (SRS) to support health information technology initiatives by generating unique ingredient identifiers (UNIs) for substances in drugs, biologics, foods, and devices.
- Non-proprietary, free, unique, unambiguous, alphanumeric identifier based on a substance's molecular structure and/or descriptive information

# UNII Assignment

- UNII, an ingredient must be a ‘substance’, which is defined as “Any physical material that has a discrete existence, irrespective of origin.”  
**Products will not be assigned a UNII.**
- More information about UNII codes and the SRS is available at:  
<http://www.fda.gov/oc/datacouncil/SRS.htm>
- Missing UNII or other terms? – Send request to [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov)

# Hyperlinks to Data Standards Manual and SPL Terminology Web Pages

- **Dosage Forms**
  - SPL web page:  
<http://www.fda.gov/oc/datacouncil/splncicodes.html#dosage>
- **Routes of Administration**
  - SPL ROA terms:  
<http://www.fda.gov/oc/datacouncil/splncicodes.html#route>
- **Units of Measure/Units of Presentation**
  - SPL web page:  
<http://www.fda.gov/oc/datacouncil/splncicodes.html#potency>
- **Colors**
  - SPL web page:  
<http://www.fda.gov/oc/datacouncil/splncicodes.html#color>
- **Shapes**
  - SPL web page:  
<http://www.fda.gov/oc/datacouncil/splncicodes.html#shape>
- **Package Types**
  - SPL web page:  
<http://www.fda.gov/oc/datacouncil/splncicodes.html#package>

# Terminology Resources

- Data Standards Manual:  
<http://www.fda.gov/cder/dsm/> (definitions of terms)
- FDA DSC SPL web page:  
<http://www.fda.gov/oc/datacouncil/spl.html>  
(acceptable terms for use in SPL documents)
- National Cancer Institute Thesaurus:  
<http://www.cancer.gov/cancertopics/terminologyresources>



# Product Types

- BULK INGREDIENT
- HUMAN OTC DRUG LABEL
- HUMAN PRESCRIPTION DRUG LABEL
- HUMAN PRESCRIPTION DRUG LABEL WITH HIGHLIGHTS
- LICENSE BLOOD INTERMEDIATES/PASTE LABEL
- LICENSED VACCINE BULK INTERMEDIATE LABEL
- NON-STANDARDIZED ALLERGENIC LABEL
- OTC ANIMAL DRUG LABEL
- OTC TYPE A MEDICATED ARTICLE ANIMAL DRUG LABEL
- OTC TYPE B MEDICATED FEED ANIMAL DRUG LABEL
- OTC TYPE C MEDICATED FEED ANIMAL DRUG LABEL
- PRESCRIPTION ANIMAL DRUG LABEL
- VACCINE LABEL
- VFD TYPE A MEDICATED ARTICLE ANIMAL DRUG LABEL
- VFD TYPE B MEDICATED FEED ANIMAL DRUG LABEL
- VFD TYPE C MEDICATED FEED ANIMAL DRUG LABEL

# Listing Data

- **Drug Listing**
- **Labeler**
  - Name
  - DUNS Number
- **Registrant**
  - Name
  - DUNS number
  - Mark as Confidential
- **Establishment**
  - Name
  - DUNS number
  - Mark as Confidential
  - Type of operation
  - Product
  - ID (section ID)
  - Effective Time

# Listing Data cont...

- **Product Information**

- Proprietary Name
- Proprietary Name Suffix
- Non-Proprietary Name
- NDC Product Code
- Dosage Form
- Source NDC Product Code (if applicable)
- DEA Schedule (if applicable)
- Route(s) of Administration

- **Active Ingredient**

- Name(s)
- Unique Ingredient Identifier(s) (UNII)
- Strength

- **Reference Drug**

- Name
- Unique Ingredient Identifier (UNII)

# Listing Data cont...

- **Active Moiety**
  - Name(s)
  - Unique Ingredient Identifier(s) (UNII)
  - Basis of Strength
- **Inactive Ingredient**
  - Name(s)
  - Unique Ingredient Identifier(s) (UNII)
  - Mark as Confidential
  - Strength
- **Flavor**
  - Name(s)
    - Original Text

# Listing Data cont...

- **Imprint Information**
  - Color(s)
    - Original Text
  - Score
  - Shape
    - Original Text
  - Imprint Code
  - Size
  - Size Unit

# Listing Data cont...

- **Packaging**
  - **Immediate packaging**
    - NDC Package Code (10 digit)
    - Quantity
    - Package Type
  - **Outer package**
    - NDC Package Code (10 digit)
    - Quantity
    - Package Type

# Listing Data cont...

- **Marketing Date**
  - Product Status
  - Start Marketing Date
  - End Marketing Date (if applicable)
- **Marketing Category**
  - Marketing Category
  - Application or citation number
  - Application or citation number code system

# **Registrant, Labeler & Establishment Info in Listing File**



# Labeler Information in Listing SPL

- Name
- DUNS number

# Labeler Information in Listing SPL

- The labeler uses their assigned NDC Labeler Code to create the NDC for the drug product. The information includes the name and DUNS Number.

**Labeler** - Labeler name here (labeler DUNS Number here)

# Registrant Information in Listing SPL

- Name
- DUNS number
- Mark as Confidential, if applicable (check box)

# Registrant Listing for PLD

- The registrant is included **if** they are listing a drug made for a private label distributor. The information includes the name and DUNS Number.
- Otherwise, do **not** complete this field

# Establishment Information in Listing SPL

- Name
- DUNS number
- Mark as Confidential (check box)
- Type(s) of operations

Establishment			
Name	Address	ID/FEI	Operations
Establishment name here		Establishment DUNS Number here	manufacture

Establishment			
Name	Address	ID/FEI	Operations
Establishment name 2 here		establishment DUNS Number here	manufacture

# Establishments in Listing SPL

- The establishments are the entities involved in the manufacturing or processing the drug product.
- Enter one or more establishments.
- The information includes the name, DUNS Number and types of operations.
  - Types of operations for an establishment in the listing SPL should also be one of the types of operations for that establishment in Establishment Registration SPL.

# Listing a API w/Finished Dosage Form Product

- Inclusion of the establishment for the API in the SPL file for the finished dosage form product. This electronically lists the API.
- Importation of API
  - The NDC for the finished product could be used for import purposes.

# Drug Listing: Establishment Information for API Manufacturers

- Establishment information for manufacturers of your **active pharmaceutical ingredient (API)** used in your products
  - Recommendation that this information **should** be included in your **electronic drug listing document** (SPL file)



# Drug Listing: Establishment Information for Inactive Ingredient Manufacturers

- Establishment information for manufacturers of **inactive ingredients** in your listed products – does **NOT** need to be included in your **electronic drug listing SPL**.

# **Product Data Elements**

# Product Data Elements

- Product
  - Product names
- Description
  - Ingredients
  - Strength
  - Dosage form
  - Route of administration
  - Controlled substance code
  - Appearance
- How supplied
  - Packaged product

**Only terms in the controlled terminology are allowed.**

# Product Name and NDC Product Code

- The proprietary/trade and ingredient name data elements only include the name and do not include any additional qualifiers such as trademark symbols, route of administration, or dosage forms. (SPL R4 only: Suffix element may contain “XL” “ER”)
- The NDC product code in SPL documents is comprised of the first two segments of the NDC

**Proprietary name: “PROPRIETARY NAME”**

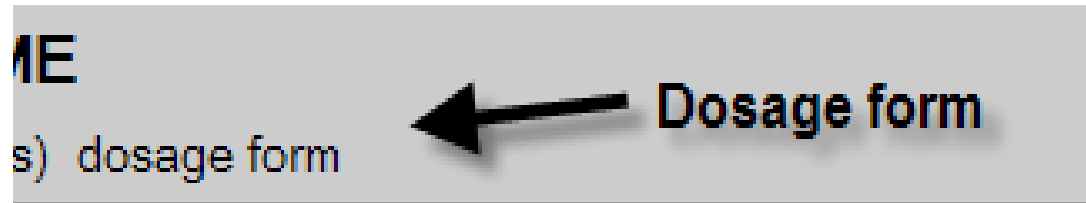
**Name of active ingredient: “name(s) of active ingredient(s)”**

**PROPRIETARY NAME**

name(s) of active ingredient(s) dosage form

# Dosage Form

- The dosage form is the name for the drug dosage form taken from the controlled terminology. Only terms in the controlled terminology are allowed.



# Route of Administration

- Labeled route of administration is the name of the route of administration taken from the controlled terminology. Only terms in the controlled terminology are allowed. A product may have one or more route of administration.

<b>Route Of Administration</b>	SUBCUTANEOUS, INTRAMUSCULAR
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# Controlled Substance Code

- The abuse potential category to which an active ingredient, or combination of active ingredients, is assigned, as regulated by both the United States Drug Enforcement Administration (DEA) and the United States Food and Drug Administration. The controlled schedule may be found near the title of the label or in the narrative portion of the label.

**DEA Schedule**

**CII**

# Active Ingredient

- The active ingredient includes the active ingredient name and identifier (Unique Ingredient Identifier (UNII) , strength, and the active moiety names and identifier (UNII). All active ingredients have at least one active moiety (in some cases two active moieties). Names of active ingredient **should not include designations such as USP or NF**. The name is taken from controlled terminology. Only terms in the controlled terminology are allowed. For ingredients, the controlled terminology is found in the FDA Substance Registration System/Ingredient Dictionary (SRS/ID). The **UNII is linked to the name** of the ingredient.
- Active moieties - more than one active moiety can be included for each active ingredient.

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
name(s) of active ingredient(s) (name of active moiety number 1 and name of active moiety number 2)	name(s) of active ingredient(s)	50 mg



# Inactive Ingredient

- The inactive ingredient includes the ingredient name, identifier, and strength. The drug listing data elements may include the inactive ingredients listed in the labeling, however, products (proprietary mixtures of ingredients such as coatings and inks), ambiguous ingredients (such as flavors and fragrances) or other “ingredients” that don’t qualify for a UNII are not included. Only the ingredient name is included in the drug listing data elements. The inactive ingredient strength is included if it is in the label.
- Mark as confidential inactive ingredients. (trade secret ingredients or other confidential ingredients not in labeling)

Inactive Ingredients	
Ingredient Name	Strength
name of inactive ingredient	

# Strength of Ingredient

## SPL Release Four

- SPL R4 documents will allow companies to **designate strength based on the active ingredient, active moiety or a reference drug.**

### Example of non-solid dosage form

Numerator: **10 mg**

Denominator: **1 mL**

### Example of solid dosage form

Numerator: **10 mg**

Denominator: **None**

# Strength cont...

Product	Numerator unit	Denominator unit
Oral solid	Weight	Each
Oral liquid	Weight	Volume
Oral powder for reconstitution with a known volume	Weight	Volume
Oral powder for reconstitution with a variable volume	Weight	Each
Suppository	Weight	Each
Injection liquid	Weight	Volume
Injection powder for reconstitution with a known volume	Weight	Volume
Injection powder for reconstitution with a variable volume	Weight	Each
Inhaler powder	Weight	Each
Inhaler liquid	Volume	Each
Inhaler blister	Weight	Each
Topical cream or ointment	Weight	Weight
Topical gel or lotion	Weight	Volume
Transdermal patch	Weight	Time
Bulk liquid	Weight	Volume
Bulk solid	Weight	Weight

# Color

- The color of the solid or liquids dosage form is the **predominant color or approximate color**, not the specification for the name in the labeling. There can be **more than one color** such as the color of the sides of a tablet and halves of capsules. **Imprints and bands on capsules are not included in the color.**
- There are **twelve SPL colors** –black, gray, white, red, purple, pink, green, yellow, orange, brown, blue, turquoise. The name is taken from these terms and only terms in the controlled terminology are allowed. **An original text field may be used to more specifically describe colors.** However, applicant should not include “cap” or “body” in the description of color. (e.g. purple cap, yellow body)

Color	WHITE (white to off-white)

# Shape

- 2-D representation of the outside perimeter of an oral solid dosage form
- **Includes rounding of corners; excludes embossing, scoring, debossing, internal cutouts**
- **19 SPL shapes:** bullet, capsule, clover, diamond, double circle, freeform, gear, heptagon, hexagon, octagon, oval, pentagon, rectangle, round, semi circle, square, tear, trapezoid, triangle.
- The name is taken from these terms and only terms in the controlled terminology are allowed. An **original text (free text) field is available to specifically describe a shape.**

<b>Shape</b>	OVAL (capsule-shaped)
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# Size

- The size is the longest single dimension for an oral solid dosage form; Length for rectangle, diameter for circle. **Millimeters rounded to the nearest millimeter**

Size	12mm
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# Score

- The score is the number of equal pieces that an oral, solid, dosage form can be divided using the score line(s).

Score

no score

Description	Value
No score	No score
Bisect (two equal pieces)	2 pieces
Trisect (three equal pieces)	3 pieces
Quadriseect (four equal pieces)	4 pieces
Unequal pieces	

# Imprint Code

- The imprint code is the alphanumeric text on solid dosage forms.  
**Includes embossed, debossed, engraved, and printed;**  
**Excludes trademark letters, marks, symbols, internal and external cutouts**
- Start top left with **semi-colon** to show separation between words or line divides

**Imprint Code**

XXX;1234



# Marketing Category

- Select the appropriate marketing category for the drug product.

Marketing Information	
Marketing Category	
NDA	

# Application or Citation Number

- Application numbers include the character application abbreviation and the numbers without spaces or dashes (e.g., NDA123456). Monograph citations include the number of the regulatory part (e.g., part234).

	Application Number or Monograph Citation
	NDA000000

# Marketing Status & Date

- The marketing status describes the activity of the product
- SPL file is removed from the public repository. The expiration date of the last lot released to the marketplace provides an estimate of the date when the SPL file is removed.

# Marketing Status & Dates

- Status of product
  - **Active:** on the market
  - **Completed:** when marketing is done the drug is no longer going to be available on the market.
  - Active or completed timestamp: effectiveTime value.
- Low value
  - Time on the market
  - Determines release of CoL/Listing SPL to public
- High value
  - Time off the market (e.g. the expiration date of the last lot released to the market.)

Marketing Start Date	Marketing End Date
01/24/2005	

# Packaging

## Single level of packaging

PACKAGING			
#	NDC	Package Description	Multilevel Packaging
1	0009-3776-01	42.5 GRAM In 1 TUBE, WITH APPLICATOR	None

## Multi-level of packaging

PACKAGING			
#	NDC	Package Description	Multilevel Packaging
1	63481-445-01	1 VIAL In 1 BOX	contains a VIAL, MULTI-DOSE
1		10 MILLILITER In 1 VIAL, MULTI-DOSE	This package is contained within the BOX (63481-445-01)

PROPRIETARY NAME - name(s) of active ingredient(s) dosage form  
Labeler

SPL Release Four Drug Listing Data Elements (Example w/Nonsolid Oral Dosage Form) - Revised Stylesheet

PROPRIETARY NAME			
name(s) of active ingredient(s) dosage form			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	NDC Product Code (Source)	0001-0001
Route of Administration	ORAL	DEA Schedule	
Active Ingredient/Active Moiety			
Ingredient Name	Basis of Strength	Strength	
name(s) of active ingredient(s) (name of active moiety number 1 and name of active moiety number 2)	name(s) of active ingredient(s)	50 mg	
Inactive Ingredients			
Ingredient Name	Strength		
name of inactive ingredient			
Product Characteristics			
Color		Score	
Shape		Size	
Flavor		Imprint Code	
Contains			
Packaging			
# NDC	Package Description	Multilevel Packaging	
1 0001-0001-02	5 mL In 1 VIAL	None	

# Drug Listing/CoL SPL Document

## MIRACLE XR

good drug tablet

### Product Information

Product Type	HUMAN PRESCRIPTION DRUG	NDC Product Code (Source)	44444-333
Route of Administration	ORAL	DEA Schedule	CII

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Good Drug (active moiety)	Good Drug	25 mg

### Inactive Ingredients

Ingredient Name	Strength
Inactive ingredient one	

### Product Characteristics

Color	yellow (yellow-orange)	Score	2 pieces
Shape	ROUND (ROUND)	Size	18mm
Flavor	CITRUS (citrus-flavored)	Imprint Code	AC;25;mg
Contains			

### Packaging

#	NDC	Package Description	Multilevel Packaging
1	44444-333-10	1 BOTTLE In 1 CARTON	contains a BOTTLE (44444-333-50)
1	44444-333-50	50 TABLET In 1 BOTTLE	This package is contained within the CARTON (44444-333-10)

# Drug Listing/CoL SPL Document

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA024380	04/13/2007	

## Labeler - Acme Pharmaceuticals, Inc (111119999)

## Establishment

Name	Address	ID/FEI	Operations
Acme Manufacturing, Inc.		475859252	manufacture

## Establishment

Name	Address	ID/FEI	Operations
Acme International		98583572	manufacture, analysis



# Common Errors in eList Pilot Program Submissions

- XML file sent not enclosed within a folder
- XML file name is not the document ID root name
- Spaces before telephone number
- Hyphens in DUNS number
- SPL file created with outdated SPL xforms
- Two-character country code used in place of three-character country code (ISO-3166 - <ftp://ftp1.nci.nih.gov/pub/cacore/EVS/FDA/SPL/>)

# eList Pilot Program Test Submissions

- Send via e-mail
- Receive feedback from FDA
- SPL e-mail account ([spl@fda.hhs.gov](mailto:spl@fda.hhs.gov))

# Delisting Products in Paper

- Lots of discontinued products to delist?
- Contact FDA at [spl@fda.hhs.gov](mailto:spl@fda.hhs.gov).

# Next Training Module

- Data Relationships
- Submitting SPL R4 v Documents via FDA Gateway

**QUESTIONS?**